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Development of a video-microscopic method to compare the effect of precipitation inhibitors

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PURPOSE

The aim of this study was to develop a microscopic method to evaluate the effect of precipitation inhibitors (PI) on supersaturated solutions of poorly soluble drugs using a digital microscopy imaging system.

METHODS

A supersaturated tadalafil solution was induced by spiking 30 µL of a 5 mg/mL DMSO stock into 200 µL fasted state simulated intestinal medium (FaSSIF, biorelevant.com) with predissolved HPMC (0-1 %w/v) as PI. The studies were performed on the oCelloScope SystemTM (Philips Biocell A/S, Allerød, DK) in a 96-well plate using video-microscopy and the precipitation was followed over time. The induction time was determined as the time point with the first particle in focus and the onwards growth of the particles was measured.

RESULTS

Without PI, the induction time was found to be 5.5 ± 1.1 minutes for tadalafil in FaSSIF. An increase in the induction time was demonstrated with increasing concentrations of HPMC, and with concentrations above 0.05 %w/v, a significantly prolonged induction time was observed (9.0 ± 1.7 to 13.6 ± 1.6 minutes, $p<0.05$). The particle growth rate slowed down in presence of HPMC. However, the growth rate was not decreased further as the HPMC concentration increased (0.01-1 %w/v). A clear difference was observed in particle size when comparing tadalafil particles with and without PI (*Fig. 1 and 2*).

CONCLUSION

Tadalafil, in presence of HPMC, shows a prolonged induction time and a reduced particle growth rate. Increasing HPMC concentrations resulted in increased induction time, but not in changes in the crystal growth rate. This method is a promising tool for comparing the effectiveness of PI on poorly soluble drugs.

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